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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,708	06/12/2001	Se-Jin Lee	JHU1320-4	7387

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,708	LEE ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *2-14* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 07/22/2004 has been entered. Claims 2-14 are pending. Claims 9, 10, 13, 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed 11/07/2002 (Paper No. 9).

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 2-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-14 are indefinite because they recite the terms "growth differentiation factor-5 (GDF-5)," "GDF-5 specific antibody," "the GDF-5 polypeptide."

Applicants argue that the term "growth differentiation factor-5 (GDF-5)" is recited in the claims preamble, that the claim body clearly defines the scope of the claimed invention, and that the claims are directed to methods of "comparing expression of growth differentiation factor-5 (GDF-5) ... having the amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13." Applicants' arguments have been fully considered but they are not persuasive. The phrase "growth differentiation factor-5 (GDF-5)" in the claim preamble sets forth the acronym "GDF-5" and it is to this acronym that the claim body refers. Therefore, the phrase "growth differentiation factor-5 (GDF-5)" in the claim preamble is considered a limitation and is of significance to claim

construction. Although the "GDF-5 specific antibody" "specifically binds a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13," the GDF-5 detected by the claimed method is not limited to "a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13." Therefore, the claims are not limited to methods of comparing expression of growth differentiation factor-5 (GDF-5) having the amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13, and the claim body does not clearly define the metes and bounds of the terms "growth differentiation factor-5 (GDF-5)," "GDF-5 specific antibody," "the GDF-5 polypeptide."

Applicants argue that the antecedent basis for the terms "said GDF-5 specific antibody" and "the GDF-5 polypeptide" is in the phrase "a GDF-5 specific antibody that specifically binds a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13," and therefore the skilled artisan would understand the meets and bounds of the claimed invention. Applicants' arguments have been fully considered but they are not persuasive. Although the "GDF-5 specific antibody" "specifically binds a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13," the GDF-5 detected by the claimed method is not limited to "a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13." Therefore, the claims are not limited to methods of comparing expression of growth differentiation factor-5 (GDF-5) having the amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13, and the claim body does not clearly define the metes and bounds of the terms "growth differentiation factor-5 (GDF-5)," "GDF-5 specific antibody," "the GDF-5 polypeptide." The examiner does not agree

that the GDF-5 detected by the claimed method is limited to "a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13."

Claims 2-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-14 are indefinite because they recite the terms "GDF-5 specific antibody" and "specifically binds" (claim 2).

Applicants argue that the terms "specific" and "specifically binds" are well understood in the art and understood to mean the ability of an antibody to distinguish a target immunogen from other antigens, as evidenced by exhibit A. Applicant's arguments have been fully considered but they are not persuasive. Although Exhibit A uses the terms "specifically," "specific," and "specificity" in relation to antibodies, Exhibit A does not provide a definition of the these terms. Therefore, Applicants' arguments are not persuasive.

Applicants argue that the examiner acknowledges that the antibody binds a GDF-5 having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13 and that a skilled artisan would clearly recognize that the terms "GDF-5 specific antibody" and "specifically binds" refer to an antibody capable of selectively binding a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13. Applicants' arguments have been fully considered but they are not persuasive. The examiner does not agree that the GDF-5 detected by the claimed method is limited to "a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13." Although the GDF-5 specific antibody binds a GDF-5 having an

amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13, the GDF-5 detected by the claimed method is not limited to a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13. Accordingly, the metes and bounds of "GDF-5 specific antibody" and "specifically binds" are not clearly set forth.

Claims 2-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2-14 are indefinite over the recitation of "altered expression" and "normal subjects" (claim 2).

Applicants argue that based only on the plain meaning of the term that it would be clear to the skilled artisan that the term "normal" refers to healthy individuals and that expression of GDF-5 in a normal subject includes expression occurring naturally and not due to disease, as evidenced by Exhibit B. Applicants argue that there is no reason to believe that that the term would be unclear to those skilled in the art and that the examiner failed to identify where in the specification the term "normal" is used in a manner that is inconsistent with its plain meaning and that there is no reason to believe the term "normal subject" would be unclear to the skilled artisan. Furthermore, Applicants' argue that the specification identifies numerous examples of "normal" individuals and the expression of GDF-5 in healthy ("normal") tissues. Applicants' arguments have been fully considered but they are not persuasive. The present specification does not set forth any "norm, rule, or principle" (Exhibit B, definition 1) with which a "normal subject" accords with, constitutes, or does not deviate from.

According to Exhibit B, definition 2, a "normal subject" would be a subject that occurs naturally and not because of disease, inoculation, or any experimental treatment. However, the specification provides no guidance that would allow those skilled in the art to determine, with a reasonable degree of confidence, whether a subject occurs naturally and how to distinguish such a naturally occurring subject from one occurring non-naturally. Exhibit B's definitions 3 and 4 are not relevant to the issue at hand. This extrinsic evidence (Exhibit B) would not provide notice to the public as to the metes and bounds of patentee's rights when the patent issues. The examiner cannot find support for "healthy" or "normal" in examples 2 and 3. One of ordinary skill in the art would not understand what is claimed, in light of the specification. Applicants' arguments concerning altered expression have been considered. However, the claims define altered expression with respect to normal subjects and the metes and bounds of normal subjects are unclear.

Claims 2-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting GDF-5 having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13 in uterine, endometrial, or skeletal tissue, does not reasonably provide enablement for detecting altered expression of GDF-5 in a person in need thereof or in the subject suspected of having altered expression of the GDF-5.

Applicants argue that the skilled artisan would have known that tissues having altered growth and differentiation would reasonably be suspected having altered expression of having altered GDF-5 expression, that the specification provides numerous

examples of disorders associated with altered expression of GDF-5, and that such roles for GDF-5 are well known in the art, as evidenced by exhibits C, D, and E. Applicant's arguments have been fully considered but they are not persuasive. Applicants' have not provided any objective evidence with which to evaluate Applicants' assertion that the skilled artisan would have known that tissues having altered growth and differentiation would reasonably be suspected having altered expression of having altered GDF-5 expression. Applicants only provide their conclusion. Nor do exhibits C, D, and E reasonably support such an assertion because there is no indication that Grebe Syndrome (Exhibit C), tendon healing (Exhibit D), or Hunter-Thompson-type dwarfism (Exhibit E) are predictive or indicative of all altered growth and differentiation in all tissues. Furthermore, the claims require that detection occur in a person in need thereof, which requires that the person be recognized as having a need for such detection. The claims encompass the detection of GDF-5 in any and/or all subjects recognized as having any disorder with which GDF-5 is associated. Yet, the specification only provides limited guidance for the detection of GDF-5 in skeletal abnormalities and uterine tissue, and lacks working examples of detection of GDF-5 in subjects in need of detecting altered expression of GDF-5. Given this limited guidance and lack of working examples, the skilled artisan is left to an undue amount of extensive experimentation involving extensive testing of any and/or all subjects and is left to determine if any and/or all of such subjects are in need of detecting altered expression of GDF-5. To practice the claimed invention in a manner consistent with the breadth of the claims would not require just a repetition of work that is described in the present application but a substantial inventive contribution on the part of a skilled practitioner which would involve the

determination of those subjects in need of detecting altered expression of GDF-5. It is this additional characterization, which is not provided for in the present specification, of that single disclosed, naturally occurring GDF5 protein and the disorders or abnormalities with which it is associated that is required in order to obtain the information needed to permit one to practice the claimed invention that constitutes undue experimentation. The skilled artisan is left to an undue amount of unduly extensive, random, trial and error experimentation in order to practice the claimed invention in a manner commensurate in scope with the claims. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Conclusion

No claims are allowable.

Claims limited to:

a method of detecting altered expression of growth differentiation factor-5 (GDF-5) in a diseased tissue comprising contacting the diseased tissue with an antibody that binds a GDF-5 polypeptide having an amino acid sequence as set forth in SEQ ID NO: 10 or SEQ ID NO: 13, or an antigen binding fragment of said antibody, and detecting binding of the antibody or the antigen binding fragment of the antibody to the diseased tissue, wherein an increased or decreased level of binding to the diseased tissue as compared to binding of the antibody to non-diseased tissue of the same type as the diseased tissue is indicative of altered expression of the GDF-5 polypeptide in the diseased tissue,

would address most, if not all, the issues raised by the examiner. However, it would raise new issues with respect to support for the claim language.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571)272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
OCTOBER 15, 2004